METHOD FOR STERILIZATION USING ETHYLENE OXIDE

TECHNICAL FIELD

The technical field includes sterilization, and more specifically industrial sterilization using ethylene oxide.

BACKGROUND

Gas sterilization is an important process for the manufacture of many industrial products. This is especially true for medical products to be used in a sterile environment.

Gas sterilization is a process for sterilizing items by exposing them to sterilizing gases, e.g. ethylene oxide (EtO or EO), for a period of time. The gas is toxic to biological organisms. To be useful, the process usually involves ensuring that no sterilizing gas residue is left on the article. Conventional gas sterilization is often performed in multiple chambers and can take many days to complete. In such a process, the product is conditioned in one chamber, sterilized (exposed to a sterilent gas) in a different chamber, and finally degassed (removal of the sterilent gas) in yet another chamber. Current single chamber sterilization processes are prolonged and sometimes not as effective as required.

It would be advantageous to simplify the gas sterilization process by reducing the time required for performing a single chamber sterilization while maintaining and enhancing the effectiveness of the process.

SUMMARY

A method for sterilizing industrial products with gas is disclosed. The method includes the step of conditioning an industrial product to be sterilized by placing the article or product to be sterilized in a chamber, evacuating the chamber, pulsing steam and/or heated inert gas into the chamber, and re-evacuating the chamber. The preferred inert gas is Nitrogen (N_2) heated to a temperature of about 130 to about 170°F. The method further includes the step of injecting a sterilent gas into the chamber. The preferred sterilent gas is ethylene oxide. Next, overpressure of inert gas is introduced into the chamber and maintained while the sterilization reaction occurs, preferably at an incremental pressure of about 5 to about 15 inches of mercury. This period of holding is sometimes referred to as the dwell time. Finally, the product is degassed.

The step of degassing the product may be accomplished by evacuating the chamber, pressurizing the chamber with about 3 to about 50 inches of mercury with an inert gas, and repeating until the product is degassed of the sterilent gas. Alternatively the step of degassing the product may be accomplished by evacuating the chamber, preferably down to a pressure in the range of 3 to 7 inches of mercury and pulsing the chamber with heated inert gas, preferably about 5 to about 9 inches of mercury worth of gas pressure. This step may be further accomplished by injecting the chamber with warm air. Warm air refers to air that is typically higher than room temperature. The exact temperature is not critical and depends on the specific article being sterilized and the sterilent gas.

Other steps may include evacuating the chamber, preferably to a pressure of about 1 to about 3 inches of mercury after the dwell time and pulsing in steam and/or heated Nitrogen into the chamber prior to degassing the product of sterilent gas. It can be advantageous to perform real-time monitoring of the concentration of ethylene oxide gas in the headspace in conjunction with the sterilization process.

Other aspects and advantages will become apparent from the following detailed description, taken in conjunction with the accompanying figures.

DETAILED DESCRIPTION

A method for sterilizing products using ethylene oxide gas in conjunction with one or more of the following techniques is disclosed: steam pulses; steam conditioning; deep vacuum pulses with nitrogen; and, positive pressure pulses of inert gases. The entire sterilization process, which generally consists of conditioning, sterilizing, and degassing the product or article, is preferably performed in a single chamber. The sterilized product is releasable to the end user from an ethylene oxide residual standpoint at the completion of the process. The entire process takes preferably less than about 10 hours, but certain applications may require up to about 20 hours or more. The method of this invention is applicable to any product suitable for ethylene oxide sterilization. The method is especially applicable to medical device products.

The sterilization method of the present invention has several steps. Each step of the method has a specific purpose and yet works cooperatively with the other steps to thoroughly and speedily sterilize products. Preferably, each step is performed in the same chamber.

However, in an alternate embodiment the entire sterilization process is performed in a continuous flow through process in which the material to be sterilized is moved through different steps in different chambers or equipment prior to completion at the end of the production line. For the preferred application of the method of the present invention, no special chamber is required. A conventional programmable industrial sterilization chamber that is equipped with a pump may be used. The pump is preferably capable of both introducing gasses into the chamber and pulling gas from the chamber to create a vacuum. The size of the chamber is not critical and depends on the scale of the load to be sterilized.

The first step in the process is referred to as the conditioning step. The purpose of the conditioning step is to raise the temperature of the product and/or introduce humidity into the chamber. Raising the temperature of the product and introducing humidity facilitates the sterilization reaction. This step may also be used to flush out air from the chamber. To begin the conditioning step, the product to be sterilized, referred to as the load, is placed in a sterilization chamber.

(Throughout the specification concentration ranges and pressure ranges are provided. These ranges are exemplary only and not intended to limit the scope of the invention. Those skilled in the art will recognize that different applications have different requirements.)

In the preferred embodiment the chamber is evacuated to a pressure of about 1 to 4 inches of mercury. After evacuation a combination of Nitrogen and steam are added into the chamber. Nitrogen is the preferred gas but any inert gas, such as helium, would be suitable. Any reference to Nitrogen includes any inert gas unless otherwise indicated. Preferably, the inert gas is heated above room temperature. Unless otherwise noted, heated inert gas is preferred throughout this specification when used.

In one aspect, first Nitrogen is injected (pushed) into the chamber then quickly removed (pulled) from the chamber, this action is commonly referred to as pulsing. Preferably, enough Nitrogen is pulsed to increase the pressure to about 2 inches of mercury and then the same amount of gas is pulled from chamber. The Nitrogen pulses may be done several times and it is preferable to do so. In one embodiment, the Nitrogen gas is heated. The preferred temperature range for the heated Nitrogen is 130 to 170°F. After the Nitrogen is pulled and the pressure is returned to near the value of the initial evacuation, i.e. a pressure of 1 to 4 inches of mercury.

In some embodiments, steam is pushed into the chamber after the inert gas is pulled out. Alternatively, the conditioning step can be performed without pulsing inert gas but only utilizing steam. The steam is pushed and pulled out of the chamber repetitively until the load is at the desired temperature and the humidity is at the desired level. In ethylene oxide sterilization, sterilization occurs at a faster rate at higher temperatures. In a typical application, the load may be sufficiently heated in less than 2 hours. In one embodiment, Nitrogen is injected over top of the steam. Preferably 10 to 20 inches of mercury of an inert gas, preferably Nitrogen, is added over top of the steam, which is believed to have the effect of forcing the steam towards the center of the load. In another embodiment a mixture of steam and inert gas are pulsed simultaneously. When the load is sufficiently conditioned, the steam and/or inert gas is again pulled out, preferably to a pressure near the initial evacuation, i.e. a pressure of about 1 to about 4 inches of mercury. At this point the sterilization step is initiated.

The sterilization step is initiated by injecting the sterilent gas into the chamber. The preferred sterilent gas is ethylene oxide. Unless otherwise indicated, any reference to ethylene gas is applicable to other sterilent gasses. Preferably, enough sterilent gas to raise the pressure about 9 inches of mercury is injected into the chamber. More or less can be injected depending on the type of sterilent gas and the product being sterilized. In a typical sterilization chamber, this would be about 400 to 550mg/L of Ethylene oxide gas, but higher or lower concentration may be used. An optional method is to inject the gas at a reduced rate than conventional processes. Rates in the range of 0.1 to 0.2 inches per minute allow the gas to more fully vaporize and gain more sensible heat, which allows for a reduced dwell time.

The load is held in the chamber until the product is sterilized. The amount of time the load is held, often referred to as the dwell time, varies depending on the product being sterilized. An inert gas overlay or inert gas blanket (also referred to as overpressure) is added to the headspace of the sterilization chamber during the dwell. Preferably Nitrogen gas overpressure is added immediately following the injection of ethylene oxide and the pressure is maintained for the duration of the dwell period. The amount of inert gas overpressure is preferably in the range of about 5 to about 15 inches of mercury, most preferably around 10-12 inches of mercury. Generally, the more overpressure added to the headspace of the

chamber, the lower the concentration of sterilent gas required and the less dwell time required to complete the sterilization.

It is believed that the inert gas overlay dynamically generates a greater surface-to-center pressure gradient on the load and shifts the highest concentration from the surface of the load towards the inside of the load. This has the effect of assisting the sterilent gas penetration into the center of the load and enhancing the uniformity of concentration distribution, thereby ensuring complete sterilization. It is also believed that the overpressure or overlay drives the steam or heated water vapor into the center of load thereby driving both heat and Ethylene oxide into the most difficult or densest areas of the product packaging configuration. This dynamic speeds what is normally considered a conventional conduction heat transfer. The presence of moisture is critical to the Ethylene oxide lethality mechanism for eradication of bacteria, yeasts & molds. The moisture coupled with the EtO are expedited to the niche areas where the bacterial flora reside thus allowing for quicker reaction time and therefore less dwell time needed to deliver the sterility necessary for the end product.

One advantage of the present invention is that the dwell time for a typical sterilization is reduced by 1/3 to 2/3 of conventional processes.

Typically, real-time measurements of the concentration of sterilent gas in the headspace is monitored during the dwell time, although not required. The preferred method of measuring and monitoring the concentration in the headspace is disclosed in U.S Patent Application No. 10/361508, which is hereby incorporated herein by reference. Measurements of the headspace concentration of ethylene oxide taken while performing the present invention show the concentration drop from 450mg/L to 150mg/L in a matter of minutes.

At the completion of the dwell period, the chamber is evacuated down to a pressure of 1 to 3 inches of mercury. An optional method is to evacuate the chamber at a reduced rate from conventional processes. Rates in the range of 0.1 to 0.5 inches per minute can enhance the residual kill. The preferred reduced evacuation rate is 0.33 inches per minute. Optionally, moisture, in the form of steam can also be injected in pulses into the chamber to aid in completing the sterilization reaction. Alternatively, heated Nitrogen may also be pulsed into the chamber, or a combination of both can be pulsed into the chamber.

When sterilization is complete the load is degassed. In general the degassing step is accomplished by evacuating the chamber and then re-pressurizing the chamber with inert gas. Preferably, the chamber is evacuated to a pressure of about 2 to 3 inches of mercury, and then re-pressurized with Nitrogen gas, preferably with enough gas to increase the pressure to about 3 to 55 inches of mercury. This step of evacuating and re-pressurizing the chamber can be repeated as many times as necessary to degas the product. Alternatively, the chamber can be evacuated to about 3 to 7 inches of mercury and pulsed with heated inert gas, preferably enough to raise the pressure about 5 to 9 inches of mercury. This step may also be repeated as necessary to degas the product. Lastly, the degassing step may include injecting the chamber with warm air. The product is released when the process has completed the validated cycle parameters. These parameters are identified and evaluated as a result of specific product and process experimental evidence to develop the exacting process parameters, which renders to the product the appropriate level of lethality and residual reduction.

Specific instructions for practicing the invention are provided in the following examples. These examples are merely illustrative and do not limit the invention in any way.

Example 1. The following procedure is used to sterilize pallets of product using EO as the sterilent gas.

Loading: Place 2 product temperature probes in the pallet at the geometrical center. Drain Vacuum pump prior to cycle start. Drain Vacuum pump during Gas dwell. Verify that all biological indicators are present on the load prior to placement into the processing chamber.

Additional: Records Product temperature prior to loading chamber (Minimum of 74F). Product temperature will be recorded throughout cycle processing. Monitor gas concentration mg/l during Gas dwell. (Minimum of 150 mg/1). After achieving pressure set point approx. 10 minutes into Gas Dwell. Load temperature at the end of Humidity Dwell 103F or greater. Load temperature throughout Gas Dwell 105F or greater. Load temperature during After Vacuum and Gas Wash A 107F or greater. Load temperature during Gas Wash B&C 98F or greater. Humidity at the end of Humidity Dwell 60% or greater. Humidity during Gas Dwell 37% or greater.

	Set Point	Minimum	Maximum

1	Load Temperature	Temperature:	74F	74F	140F
2	Process Temperature		130F	120F	140F
3	Initial Vacuum	Evacuate To:	2.0"HgA	2.5"HgA	1.5"HgA
4	Approx. Rate: 1.0"Min	Time:	40 Min	25 Min	90 Min
5	Humidification		1.0"Hg-Rise	0.5"Hg-Rise	1.5"Hg-Rise
6	Approx. Rate: NA	Time:	NA	NA	NA
7	Steam Conditioning	Humidity To:	3.0"HgA	2.5"HgA	3.5"HgA
8		Evacuate To:	2.5"HgA	3.0"HgA	2.0"HgA
9		Dwell Time:	60 Min	50 Min	80 Min
10	Humidity Dwell	Dwell Time:	15 Min	15 Min	25Min
11		Maintain Pressure At:	3.0"HgA	2.5"HgA	3.5"HgA
12	Gas Inject	Gas By Weight:	NA	NA	NA
13	<u>Inject Type</u>	Drum Change Allowed? Yes			
14		Gas To:	11.2"HgA	10.7"HgA	11.7"HgA
15	Approx. Rate: 0.5"/Min	Time:	20 Min	8 Min	45 Min
16	Parametric Release	Gas Con.:	150 MG/L	150 MG/L	542MG/L
17		Gas Dwell) Load Temperature:	F	105F	140F
18		(Gas Dwell) Load Relative Humidity:	%	37%	%
19	Gas Dwell	Temperature:	130F	125F	140F
20		Time:	1 Hrs 40 Min	1 Hrs 39 Min	1 Hrs 50Min
21	Maintain Pressure With:	N2 At:	23.2"HgA	22.7"HgA	25.9"HgA
22					
23	After Vacuum	Evacuate To:	2.5"HgA	3"HgA	2"HgA
24	Approx. Rate: .33"/Min	Time:	65 Min	58 Min	180 Min
25		Vacuum Hold Time:	NA	NA	NA
26					
27	Gas Wash A	Inject To:	3.0"HgA	2.5"HgA	3.5"HgA
28	Approx. Rate: 1 "/Min	Time:	1 Min	0.3/9 Min	2/30 Min
29	<u>Inject Type:</u>	Evacuate To:	2.7"HgA	3.2"HgA	2.2"HgA
30	Steam				
31	Approx. Rate: NA "/Min	Time:			
32		Vacuum Hold Time:	NA	NA	NA
33	Number of Repeats: 4(5Total)				
34					
35	Gas Wash B	Inject To:	26.0"HgA	25.5"HgA	26.5"HgA
36	Approx. Rate: 1 "/Min	Time:	24 Min	18 Min	40 Min
37	<u>Inject Type:</u>	Evacuate To:	3.0"HgA	3.5"HgA	2.5"HgA
38	N2				
39	Approx. Rate: 1 "/Min	Time:	24 Min	18/139 Min	40/240 Min
40		Vacuum Hold Time:	NA	NA	NA
41	Number of Repeats: 2(3Total)				
42					
43	Gas Wash C	Inject To:	26.0"HgA	25.5"HgA	26.5"HgA
44	Approx. Rate: 1 "/Min	Time:	24 Min	18 Min	40 Min
45	<u>Inject Type:</u>	Evacuate To:	3.0"HgA	3.5"HgA	2.5"HgA
46	Air				
47	Approx. Rate: 1 "/Min	Time:	24 Min	18/323 Min	40/560 Min
48		Vacuum Hold Time:	NA	NA	NA

Number of Repeats: 6 (7Total)				
Final Release	Release To:	28.0"HgA	27.5"HgA	NA"HgA
Approx. Rate: 1.0 "/Min	Time:	26 Min	20 Min	60 Min

Example 2: The following procedure is used to sterilize 30 pallets of product using EO as the sterilent gas.

Preprocessing: Probes (Internal Temperature) will be placed in pallet #s 1, 8 and 15 prior to loading chamber. Temperature must be 75 F. If temperature is below 75 F, the load will be placed load in a preheating room to bring the temperature to specification. Plug in product thermocouples and place between cases in middle pallets 1 and 16. All loads will consist of 30 pallets.

Loading: All pallets will be loaded in descending order with pallets 1 – 15 on the right side of the chamber and 16 – 30 on the left side of the chamber.

Other: 1) Parametric Release Criteria:

1.1) A temperature probe will be placed in pallet #1 and pallet #16 (geometric centers) to monitor load temperature during ETO Gas dwell and steam temperature

1.2) EO Concentration must meet minimum requirement after N_2 injection.

2) Maximum temperature during washes is 150.

		Set Point	Minimum	Maximum
Load Temperature	Temperature:	75F	75F	N/A
Process Temperature		135F	125F	145F
Initial Vacuum	Evacuate To:	2.0"HgA	1.5"HgA	2.5"HgA
Approx. Rate: 1.0"Min	Time:	N/A	N/A	N/A
Nitrogen Wash	Humidity To:	N/A	N/A	N/A
	N_2 Inject To:	12.0"HgA	11.5"HgA	12.5"HgA
Approx. Rate: N/A	Time:	N/A	N/A	N/A
Number of Repeats				
One Total	Evacuate To:	2.8"HgA	2.3"HgA	3.3"HgA
Approx. Rate: N/A	Time:	N/A	N/A	N/A
Humidification		N/A"HgA	N/A"HgA	N/A"HgA
Approx. Rate: NA	Time:	NA	NA	NA

Steam Conditioning	Humidity To:	2.8”HgA	2.3”HgA	3.3”HgA
	Evacuate To:	2.2”HgA	1.7”HgA	2.7”HgA
	Dwell Time:	90 Min	85 Min	120 Min
Humidity Dwell	Dwell Time:	10 Min	10 Min	15Min
	Maintain Pressure At:	2.8”HgA	2.3”HgA	3.3”HgA
Gas Inject	Gas By Weight:	NA	NA	NA
Inject Type	Drum Change Allowed? Yes			
	Gas To:	12.9”HgA	12.4”HgA	13.4”HgA
Approx. Rate: 1.0”/Min	Time:	N/A	N/A	N/A
Parametric Release	Gas Con.:	550 MG/L	350 MG?	750MG/L
Gas Dwell	Temperature:	135F	130F	145F
	Time:	2 Hrs 30 Min	2 Hrs 30 Min	2 Hrs 35Min
Maintain Pressure With:	Inert At:	25.0”HgA	24.0”HgA	28.0”HgA
After Vacuum	Evacuate To:	3.0”HgA	2.0”HgA	4.0”HgA
Approx. Rate: 0.3”/Min	Time:	N/A	N/A	N/A
	Vacuum Hold Time:	N/A	NA	NA
Gas Wash A	Inject To:	50”HgA	49.5”HgA	50.5”HgA
Approx. Rate: 2.0 “/Min	Time:	N/A	N/A	N/A
Inject Type:	Evacuate To:	3.0”HgA	2.5”HgA	3.5”HgA
Inert				
Approx. Rate: 0.4“”Min	Time:	N/A	N/A	N/A
	Vacuum Hold Time:	15 Min	15 Min	20 Min
Number of Repeats: Four total				
Gas Wash B	Inject To:	12.0”HgA	11.5”HgA	12.5”HgA
Approx. Rate: 2.0 “/Min	Time:	N/A	N/A	N/A
Inject Type:	Evacuate To:	1.0”HgA	0.5”HgA	1.5”HgA
Air				
Approx. Rate: 0.4“/Min	Time:	N/A	N/A	N/A
	Vacuum Hold Time:	5 Min	5 Min	10 Min
Number of Repeats: One Total)				
Gas Wash C	Inject To:	25.0”HgA	24.5”HgA	25.5”HgA
Approx. Rate: 2.0 “/Min	Time:	N/A	N/A	N/A
Inject Type:	Evacuate To:	1.5”HgA	1”HgA	2”HgA
Air				
Approx. Rate: 0.4“/Min	Time:	N/A	N/A	N/A
	Vacuum Hold Time:	5 Min	5 Min	10 Min
Number of Repeats: One Total				